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Process for the production of 4-hydroxybenzaldehyde derivatives

This invention relates to a process for the production of 4-hydroxybenzaldehyde derivatives by oxidizing a p-cresol derivative with oxygen or a free oxygen-containing gas in the presence of a base and a cobalt compound or metallic cobalt.

The 4-hydroxybenzaldehyde derivatives are not only important starting materials for organic chemistry but are also useful compounds with a wide variety of applications including use as flavoring agents. For example, 4-hydroxybenzaldehyde and 3,5-di-tert-butyl-4-hydroxybenzaldehyde are important intermediates for the preparation of pharmaceuticals or agricultural chemicals, while 3-alkoxy-4-hydroxy-benzaldehydes are useful as vanillin flavorings.

Several methods are known for the production of 4-hydroxybenzaldehyde derivatives. One of these methods comprises oxidizing a corresponding p-cresol derivative with oxygen. This reaction could become an advantageous method, if a selective oxidation to the corresponding 4-hydroxybenzaldehyde were achieved in a high yield by using a suitable catalyst. This oxidation reaction, however, involves the following problems. Firstly, oxidation of the benzene nucleus may be more rapid than the oxidation of the methyl group in the p-cresol derivative. Particularly, in the case of a p-cresol derivative having no substituent at the ortho-position to the hydroxyl group, it is known that the coupling at the ortho-position becomes the principal reaction (see for example R. F. Moore and W. A. Waters: J. Chem. Soc., 1954, 243). It is also known that in the oxidation of an aromatic compound having a methyl group, such as for example toluene, xylene, etc., the corresponding carboxylic acid is produced via the formation of an aldehyde. Thus, generally, the oxidation rate of an aldehyde group is far higher than that of a methyl group, and it is difficult to obtain an aromatic aldehyde in a high yield using an oxidation method.

For these reasons only the following two methods are at present available for the selective production of 4-hydroxybenzaldehyde derivatives by oxidation of the corresponding p-cresol derivatives.

(1) An oxidation method using potassium tertiary butoxide in dimethylformamide (A. Nishinaga, T. Itahara and T. Matsuura: Angew. Chem., internat. Edit., Vol. 14 (1975), 356).

This method requires the use of a specific solvent and a large excess of the base; moreover the use of other starting materials than 2,6-di-substituted p-cresols results in a very poor yield of the aldehyde.

(2) An oxidation method using an N,N'-ethylenebis-(salicylidene iminate)cobalt (II) catalyst in an alcohol as solvent or using a cuprous chloride catalyst in a pyridine as solvent (T. Shimizu, A. Nishinaga and T. Matsuura: A Collection of Abstracts of the Lectures at 12th Oxidation Reaction Forum, p. 74, 1978, Tokyo).

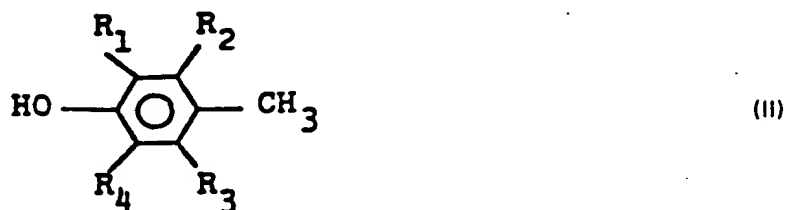
This method also uses 2,6-di-substituted p-cresols as starting material and requires the use of a specific solvent and a large amount of catalyst, making its industrial application impractical.

In order to overcome these problems, the present inventors have done further research into developing a method for the selective preparation of 4-hydroxybenzaldehyde derivatives in high yield by oxidation of p-cresol derivatives in a wider range including 2,6-unsubstituted p-cresol derivatives; the present invention solves this problem.

Thus, the present invention relates to a process for the production of 4-hydroxybenzaldehyde derivatives of the formula:



wherein each of R₁, R₂, R₃ and R₄ is selected from the group consisting of hydrogen atom, halogen atoms, lower alkyl groups, cyclohexyl group, lower alkoxy groups and cyclohexyloxy group which comprises the reaction of a p-cresol derivative of the formula:



wherein each of R_1 , R_2 , R_3 and R_4 is as defined above with oxygen or a free oxygen-containing gas in a solvent which is stable to oxygen in the presence of a base having a higher basicity than the p-cresol derivative of the formula (II) and a catalytic amount of a cobalt compound or metallic cobalt.

The process of this invention has the following salient features and advantages:

- 5 (1) The starting material used in this invention is open to a wider choice. It is possible according to the process of this invention to oxidize even the p-cresol derivatives having no substituent at the ortho-position to the hydroxyl group, for example p-cresol itself.
- (2) The yield of the produced 4-hydroxybenzaldehyde derivative is higher than that obtainable from the aforementioned two conventional methods.
- 10 (3) Only the methyl group at the para-position of the hydroxyl group is selectively oxidized to a formyl group while the other substituents R_1 , R_2 , R_3 and R_4 remain unchanged.
- (4) Mixed cresol derivatives can be conveniently used as starting material (II). For example, the process of the present invention can be carried out using a mixture of m- and p-cresols to obtain 4-hydroxybenzaldehyde as well as unchanged m-cresol.
- 15 (5) A wide variety of cobalt compounds can be used as catalyst, and no specific compound is required. Also, the amount of such cobalt compound used is minimized.
- (6) Selection of the solvent is not subject to any specific restrictions, and a wider range of choice is possible.

The invention is now described in further detail.

- 20 As for the substituents R_1 , R_2 , R_3 and R_4 in the p-cresol derivatives of the formula (II) used as starting material in this invention, the halogen atom may be fluorine, chlorine, bromine or iodine, but chlorine and bromine are preferred. The lower alkyl groups usable in this invention have 1 to 6, preferably 1 to 4, carbon atoms, and include methyl group, ethyl group, propyl group, isopropyl group, n-butyl group, secondary butyl group, isobutyl group, tertiary butyl group, cyclohexyl group and the like.
- 25 The lower alkoxy groups usable in this invention have 1 to 6, preferably 1 to 4, carbon atoms and include methoxy group, ethoxy group, propoxy group, isopropoxy group, n-butoxy group, secondary butoxy group, isobutoxy group, tertiary butoxy group, cyclohexyloxy group and the like. More specific examples of the p-cresol derivatives of the general formula (II) include p-cresol, 2,6-dichloro-p-cresol, 2-bromo-p-cresol, mesitol, 2,4-xlenol, 3,4-xlenol, 2,6-di-tert-butyl-p-cresol, 2-methoxy-p-cresol, 2,6-dimethoxy-p-cresol, 2-ethoxy-p-cresol, 2-chloro-p-cresol, 2,6-dibromo-p-cresol and 2-tert-butyl-p-cresol.

- Examples of the p-hydroxybenzaldehyde derivatives of the formula (I) produced by oxidation of said p-cresol derivatives in accordance with the present invention are 4-hydroxybenzaldehyde, 3,5-dichloro-4-hydroxybenzaldehyde, 3-bromo-4-hydroxybenzaldehyde, 3,5-dimethyl-4-hydroxybenzaldehyde, 4-hydroxy-3-methylbenzaldehyde, 4-hydroxy-2-methylbenzaldehyde, 3,5-di-tert-butyl-4-hydroxybenzaldehyde, vanillin, 3,5-dimethoxy-4-hydroxybenzaldehyde, ethyl-vanillin, 3-chloro-4-hydroxybenzaldehyde, 3,5-dibromo-4-hydroxybenzaldehyde, and 3-tert-butyl-4-hydroxybenzaldehyde, respectively.

- 40 The cobalt atom contained in the cobalt compound used as catalyst in this invention may be either zero-, di- or trivalent. Various types of cobalt compounds may be used in this invention, for example cobalt halide such as cobalt fluoride, cobalt chloride, cobalt bromide, cobalt iodide, etc., salts of cobalt with organic acids such as cobalt acetate, cobalt octylate, cobalt stearate, cobalt oxalate, cobalt naphthenate, cobalt resinate, salts of cobalt with inorganic acids such as cobalt nitrate, cobalt sulfate, cobalt borate, cobalt carbonate, cobalt cyanide, cobalt phosphate, etc., cobalt oxides such as sulfate, cobalt borate, cobalt sesquioxide, tricobalt tetraoxide, etc., cobalt hydroxide and metallic cobalt.
- 45 Cobalt complexes such as cobalt chelates are also effective as catalyst in this invention. Examples of such cobalt complexes are cobalt acetylacetonate, bis(dimethylglyoximate) cobalt, cobalt porphyrin, N,N'-ethylenebis(salicylidene imine)cobalt and N,N'-ethylenebis(3-ethoxysalicylidene imine)cobalt. Among these cobalt compounds, hydrates or anhydrides of salts such as cobalt hydroxide, cobalt oxides, cobalt chloride, cobalt bromide, cobalt acetate, cobalt naphthenate, cobalt oxalate, cobalt sulfate, cobalt nitrate, etc., and metallic cobalt are most preferred.

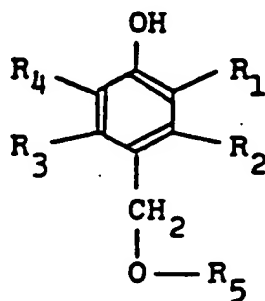
- 50 The amount of the cobalt compound used is not subject to any specific restriction. A molar ratio of the cobalt compound to the p-cresol derivative or a ratio of the metallic cobalt in gram atoms to the moles of the p-cresol derivative of not less than 0.0001:1 will do, but a range of 0.0005:1 to 0.05:1 is preferred.

- 55 Any type of base having a higher basicity than the p-cresol derivative of the formula (II) may be used in this invention. Examples of such bases are metal hydroxides such as sodium hydroxide, potassium hydroxide, lithium hydroxide, magnesium hydroxide, calcium hydroxide, aluminum hydroxide, etc., metal alkoxides such as sodium alkoxide, potassium alkoxide, lithium alkoxide, magnesium alkoxide, calcium alkoxide, aluminum alkoxide, etc. (the alkoxide used here may be, for example, methoxide, ethoxide, isopropoxide, tertiary butoxide, etc.), and metal amides such as lithium amide, sodium amide, potassium amide, etc. (the amide used here may be, for example, unsubstituted amide, ethylamide, diethylamide, diisopropylamide, etc.). Among the above-mentioned bases, sodium hydroxide, potassium hydroxide, sodium methoxide, potassium methoxide, sodium ethoxide, potassium ethoxide, potassium tertiary butoxide and sodium amide are preferred.
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The amount of the base used is selected without particular limitation provided that the molar ratio of the base to the p-cresol derivative of the formula (I), is not less than 1:1, a range of 1:1 to 10:1 is preferred.

Various types of solvents, which are stable to oxygen and are capable of dissolving the starting material, may be used in the reaction of this invention. Preferred examples of such solvents are alcohols, hydrocarbons, ethers, halogenated hydrocarbons, amines, dimethylformamides, dimethylsulfoxides and the like. These solvents may be used either singly or in admixture of two or more. They may be diluted with water. Most preferred among these solvents are alcohols such as methanol, ethanol, isopropanol, butanol, tertiary butanol, ethylene glycol, etc.

In connection with this invention, the present inventors have found the following new facts: When using an alcohol represented by the formula: R_5OH (wherein R_5 is a lower alkyl group such as a methyl, ethyl, isopropyl or butyl group) as solvent in practising the process of this invention, a corresponding p-alkoxymethylphenol derivative represented by the formula (III):



(III)

(wherein R_1 , R_2 , R_3 , R_4 and R_5 are as defined above) results as by-product. It was also confirmed that the compound of the formula (III) is further oxidized under the reaction conditions of this invention to give the corresponding 4-hydroxybenzaldehyde derivative of the formula (I) which is the final product.

In the process of this invention, oxygen (oxidizing agent) may be used either singly as it is or after diluting it with a so-called inert gas (such as nitrogen or argon gas) to form a free oxygen-containing gas. Air may also be used as a free oxygen-containing gas.

Although no particular restriction is imposed on the pressure of oxygen or oxygen-containing gas to be used, a pressure between 1 and 100 bar is preferred.

The oxygen content in the free oxygen-containing gas is also not subject to any specific limitation; such content may be suitably determined by taking into account such matters as safety of the operation and reaction rate.

The reaction temperature may be selected from within the range of 0 to 300°C, but the range of from room temperature to 200°C is advisable to ensure a sufficiently high reaction rate.

Recovery of the starting material from the reaction mixture and isolation and purification of the object product may be accomplished by employing commonly used methods such as concentration of the reaction mixture, acidification of the residue, extraction with an organic solvent, concentration or distillation of the extract, etc. In case the obtained 4-hydroxybenzaldehyde derivative cannot be distilled, recrystallization or sublimation may be employed.

The process of this invention is described in further detail hereinbelow by way of the following examples, which are only illustrative and are not intended to limit the scope of this invention.

Example 1

A mixture consisting of p-cresol (6.0 g, 55.6 mmol), cobalt (II) chloride (0.072 g, 0.556 mmol), sodium hydroxide (6.67 g, 168 mmol) and methanol (18 ml) was stirred in an oxygen atmosphere of 1 bar at 60°C for 6 hours (stirring rate: 800—1,000 rpm).

After distilling off methanol from the reaction mixture under reduced pressure, dilute hydrochloric acid was added to the residue to make it acidic and the product was extracted with ethyl acetate. The extract composition, as analyzed by gas chromatography, was made up as follows:

p-cresol: 0.480 g; recovery: 8%; conversion: 92%
p-methoxymethylphenol: 0.141 g; selectivity: 2%
4-hydroxybenzaldehyde: 4.86 g; selectivity: 78%

$$\text{Conversion (\%)} = \frac{\text{Moles of p-cresol consumed}}{\text{Moles of p-cresol used}} \times 100$$

$$\text{Selectivity (\%)} = \frac{\text{Moles of product}}{\text{Moles of p-cresol consumed}} \times 100$$

Example 2

Example 1 was repeated, except that air (free of carbon dioxide gas and moisture) was blown into the mixture at the rate of 250 ml/min instead of using an oxygen atmosphere, and the reaction was carried out at 60°C for 10 hours.

The reaction mixture was treated in the same way as Example 1 to obtain the following results:

p-cresol conversion: 95%
4-hydroxybenzaldehyde selectivity: 79%
4-methoxymethylphenol selectivity: 3%

Examples 3—11

Cobalt (II) chloride (0.072 g, 0.556 mmol), bases shown in Table 1 (in amounts also shown in Table 1) and solvents shown in Table 1 (in amounts also shown in Table 1) were added to p-cresol (6.0 g), and each of the obtained mixtures was vigorously stirred in an oxygen atmosphere of 1 bar at a temperature shown in Table 1 for 6 hours. The reaction mixture was treated in the same way as Example 1, and the product was analyzed by gas chromatography. Conversion of p-cresol and selectivity of 4-hydroxybenzaldehyde (represented by A) and p-alkoxymethylphenol (represented by E; the alkoxy group is one which is derived from the alcohol used as solvent) are shown in Table 1.

TABLE 1

Example	Base (amount used, g)	Solvent (amount used, ml)	Temp. (°C)	Conversion (%)	Selectivity (%)	
					A	E
3	Sodium hydroxide (4.44)	Methanol (12)	60	87	73	1
4	Sodium hydroxide (3.33)	Methanol (9)	60	49	69	4
5	Potassium hydroxide (9.33)	Methanol (18)	60	92	76	2
6	Sodium methoxide (9.00)	Methanol (18)	60	90	68	10
7	Potassium methoxide (11.7)	Methanol (18)	60	92	75	5
8	Sodium hydroxide (6.67)	Ethanol (18)	60	59	51	3
9	Potassium tertiary butoxide (18.7)	Tertiary butanol (18)	60	68	52	0
10	Sodium hydroxide (6.67)	Ethylene glycol (36)	60	82	55	—
11	Sodium hydroxide (6.67)	Methanol (18)	50	61	71	7

Examples 12—21

Sodium hydroxide (7.02 g), methanol, (18 ml) and cobalt compounds shown in Table 2 (in amounts also shown in Table 2) were added to p-cresol (6.0 g), and each of the obtained mixtures was stirred in an oxygen atmosphere of 1 bar at 60°C for a period shown in Table 2. The reaction mixture was treated in the same way as Example 1 and the product was analyzed by gas chromatography, obtaining the results shown in Table 2. Stirring was performed by using a motor in Examples 12—18 and a magnetic stirrer in Examples 19—21.

TABLE 2

Example	Cobalt compound (Amount used mg)	Time (hr.)	Conversion (%)	Selectivity (%)	
				A	E
12	Cobalt (II) chloride (36)	6	92	75	2
13	Cobalt (II) chloride (7.2)	6	89	72	3
14	Cobalt (II) acetate (98)	6	93	75	4
15	Cobalt (II) sulfate heptahydrate (156)	6	90	71	6
16	Cobalt (II) nitrate hexahydrate (162)	6	91	70	3
17	Cobalt (II) hydroxide (52)	6	64	65	6
18	Cobalt (III) hydroxide oxide (51)	6	86	78	3
19	Cobalt (II) monoxide (204)	40	87	52	8
20	Cobalt (III) sesquioxide (231)	40	82	52	9
21	Metallic cobalt (164)	40	89	53	10

Example 22

A mixture consisting of 2-methoxy-p-cresol (6.0 g, 43.5 mmol), cobalt (II) chloride (0.057 g, 0.435 mmol), sodium hydroxide (5.22 g, 131 mmol) and methanol (14 ml) was vigorously stirred in an oxygen atmosphere of 1 bar at 60°C for 6 hours. The reaction mixture was treated in the same manner as in Example 1 and the product was analyzed by gas chromatography. The starting materials were completely used up and formation of the following compounds was determined.

Vanillin (3.97 g; yield: 60%)

2-methoxy-4-methoxymethylphenol (0.51 g; yield: 7%)

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Examples 23—33

Mixtures consisting of p-cresol derivatives (50 mmol) shown in Table 3, cobalt (II) chloride (0.5 mmol), sodium hydroxide (150 mmol) and methanol (16 ml) were vigorously stirred in an oxygen atmosphere of 1 bar at 60°C for the periods shown in Table 3. The respective reaction mixtures were treated in the same way as Example 1 and the products were analyzed by gas chromatography. Conversions of the respective p-cresol derivatives and selectivities of the respective 4-hydroxybenzaldehyde derivatives were as shown in Table 3.

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TABLE 3

Example	Substituents in formulae (I) and (II)				Reaction time (hr.)	p-cresol derivatives of formula (II)	Conversion (%)	4-hydroxybenzaldehyde derivatives of formula (I)	Selectivity (%)
	R ₁	R ₂	R ₃	R ₄					
23	Cl	H	H	H	6	2-chloro-p-cresol	70	3-chloro-4-hydroxybenzaldehyde	63
24	Br	H	H	H	6	2-bromo-p-cresol	65	3-bromo-4-hydroxybenzaldehyde	66
25	Me	H	H	H	6	2,4-xyleneol	100	4-hydroxy-3-methylbenzaldehyde	66
26	H	Me	H	H	6	3,4-xyleneol	100	4-hydroxy-2-methylbenzaldehyde	62
27	Me	H	H	Me	4	Mesityl	100	3,5-dimethyl-4-hydroxybenzaldehyde	59
28	t-Bu	H	H	H	6	2-tert-butyl-p-cresol	100	3-tert-butyl-4-hydroxybenzaldehyde	58
29	t-Bu	H	H	t-Bu	0.5	2,6-di-tert-butyl-p-cresol	100	3,5-di-tert-butyl-4-hydroxybenzaldehyde	52
30	OEt	H	H	H	6	2-ethoxy-p-cresol	100	Ethyl vanillin	61
31	OMe	H	H	OMe	2	2,6-dimethoxy-p-cresol	100	3,5-dimethoxy-4-hydroxybenzaldehyde	55
32	Cl	H	H	Cl	6	2,6-dichloro-p-cresol	60	3,5-dichloro-4-hydroxybenzaldehyde	70
33	Br	H	H	Br	6	2,6-dibromo-p-cresol	58	3,5-dibromo-4-hydroxybenzaldehyde	68

Example 34

Into a mixed cresol consisting of 30% of m-cresol and 70% of p-cresol (8.57 g, 79.4 mmol) were added cobalt (II) chloride (0.072 g, 0.556 mmol), sodium hydroxide (6.67 g, 168 mmol) and methanol (18 ml), and the resulting mixture was vigorously stirred in an oxygen atmosphere of 1 bar at 65°C for 5 hours.

The reaction mixture was treated in the same manner as in Example 1, and the composition of the product, as analyzed by gas chromatography, was as follows:

Recovery of m-cresol: 90%,
Conversion of p-cresol: 82%,
Selectivity of 4-hydroxybenzaldehyde: 72%,
Selectivity of 4-methoxymethylphenol: 2%.

The reaction mixture contained neither 3-hydroxybenzaldehyde nor 3-methoxymethylphenol.

Referential Example 1

Oxidation of m-cresol was carried out and the reaction mixture was treated and analyzed in the same manner as in Example 1. As a result, 99% of m-cresol was recovered, and no formation of 3-hydroxybenzaldehyde was seen.

Referential Example 2

Oxidation of o-cresol was carried out and the reaction mixture was treated and analyzed in the same manner as in Example 1. As a result, 80% of o-cresol was recovered and the production of salicylaldehyde was less than 1%.

Claims

1. A process of the production of 4-hydroxybenzaldehyde derivatives of the formula:



wherein each of R₁, R₂, R₃ and R₄ is selected from the group consisting of hydrogen atom, halogen atoms, lower alkyl groups, cyclohexyl group, lower alkoxy groups, and cyclohexyloxy group, characterized by reacting a p-cresol derivative of the formula:



wherein each of R₁, R₂, R₃ and R₄ is as defined above, with oxygen or a free oxygen-containing gas in a solvent which is stable to oxygen and which is capable of dissolving the starting material in the presence of a base having a higher basicity than the p-cresol derivative of the formula (II) and a catalytic amount of a cobalt compound or metallic cobalt.

2. The process according to claim 1, characterized by carrying out the reaction with p-cresol, 2-bromo-p-cresol, 2-chloro-p-cresol, 2,6-dibromo-p-cresol, 2,6-dichloro-p-cresol, 2,4-xyleneol, 3,4-xyleneol, mesitol, 2-*t*-butyl-p-cresol, 2,6-di-*t*-butyl-p-cresol, 2-methoxy-p-cresol, 2-ethoxy-p-cresol or 2,6-dimethoxy-p-cresol as a p-cresol derivative.

3. The process according to claim 1, characterized by carrying out the reaction with sodium hydroxide, potassium hydroxide, sodium methoxide, potassium methoxide, sodium ethoxide, potassium ethoxide, potassium *t*-butoxide or sodium amide as a base.

4. The process according to claim 1, characterized by carrying out the reaction with cobalt hydroxide, a cobalt oxide, cobalt chloride, cobalt acetate, cobalt sulfate or cobalt nitrate as a cobalt compound.

5. The process according to claim 1, characterized by carrying out the reaction in methyl alcohol, ethyl alcohol, isopropyl alcohol, *t*-butyl alcohol or ethylene glycol as solvent.

6. The process according to claim 1, characterized by carrying out the reaction with a molar ratio of the base to the *p*-cresol derivative in the range of 1:1 to 10:1.

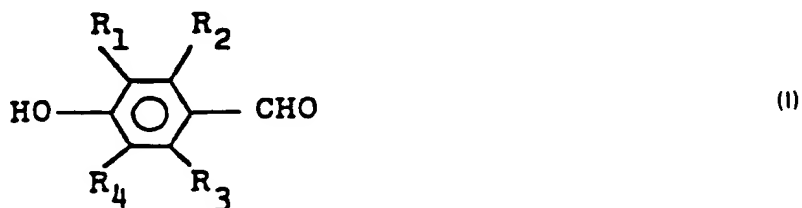
7. The process according to claim 1, characterized by carrying out the reaction with a cobalt compound or metallic cobalt as catalyst, the molar ratio of the cobalt compound to the *p*-cresol derivative, or the ratio of the metallic cobalt in gram atoms to the moles of the *p*-cresol derivative being in the range of 0.0005:1 to 0.05:1.

8. The process according to claim 1, characterized by carrying out the reaction at a temperature in the range of 20 to 200°C.

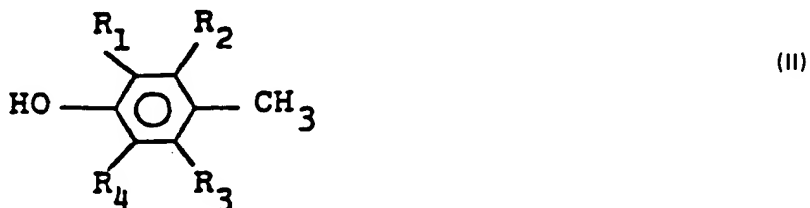
9. The process according to claim 1, characterized by carrying out the reaction with air or a mixture of oxygen and nitrogen as a free oxygen-containing gas.

Revendications

1. Procédé pour la production de dérivés du 4-hydroxybenzaldéhyde de formule



dans laquelle chacun des radicaux R_1 , R_2 , R_3 et R_4 est choisi dans le groupe constitué par un atome d'hydrogène, des atomes d'halogènes, des groupes alcoyle inférieur, le groupe cyclohexyle, des groupes alcoxy inférieur et le groupe cyclohexyloxy, caractérisé en ce qu'on fait réagir un dérivé du *p*-crésol de



dans laquelle chacun des radicaux R_1 , R_2 , R_3 et R_4 a la signification donnée ci-dessus, avec l'oxygène ou un gaz contenant de l'oxygène libre, dans un solvant qui est stable à l'oxygène et qui est capable de dissoudre la substance de départ, en présence d'une base ayant une basicité plus élevée que le dérivé du *p*-crésol de formule (II) et en présence d'une quantité catalytique d'un composé du cobalt ou de cobalt métallique.

2. Procédé selon la revendication 1, caractérisé en ce que la réaction est menée avec le *p*-crésol, le 2-bromo-*p*-crésol, le 2-chloro-*p*-crésol, le 2,6-dibromo-*p*-crésol, le 2,6-dichloro-*p*-crésol, le 2,4-xylénol, le 3,4-xylénol, le mésitol, le 2-tertiobutyl-*p*-crésol, le 2,6-ditertiobutyl-*p*-crésol, le 2-méthoxy-*p*-crésol, le 2-éthoxy-*p*-crésol ou le 2,6-diméthoxy-*p*-crésol, en tant que dérivé du *p*-crésol.

3. Procédé selon la revendication 1, caractérisé en ce que la réaction est menée avec l'hydroxyde de sodium, l'hydroxyde de potassium, le méthoxyde de sodium, le méthoxyde de potassium, l'éthoxyde de sodium, l'éthoxyde de potassium, le tertibutoxyde de potassium ou un amide de sodium, en tant que base.

4. Procédé selon la revendication 1, caractérisé en ce que la réaction est menée avec l'hydroxyde de cobalt, un oxyde de cobalt, le chlorure de cobalt, l'acétate de cobalt, le sulfate de cobalt ou le nitrate de cobalt, en tant que composé du cobalt.

5. Procédé selon la revendication 1, caractérisé en ce que la réaction est menée dans l'alcool-méthyllique, l'alcool éthylique, l'alcool isopropylique, l'alcool tertibutylique ou l'éthylèneglycol, en tant que solvant.

6. Procédé selon la revendication 1, caractérisé en ce que la réaction est menée avec un rapport molaire de la base au dérivé du *p*-crésol compris entre 1:1 et 10:1.

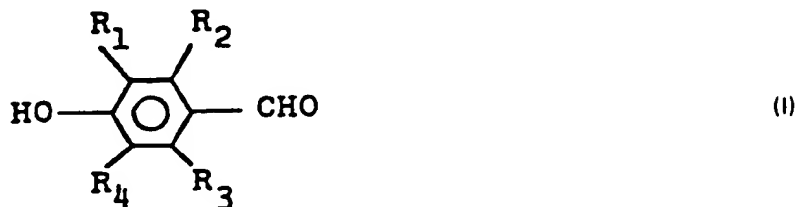
7. Procédé selon la revendication 1, caractérisé en ce que la réaction est menée avec un composé du cobalt ou le cobalt métallique en tant que catalyseur, le rapport molaire du composé du cobalt au dérivé du *p*-crésol ou le rapport du cobalt métallique en atomes-grammes aux moles du dérivé du *p*-crésol se situant dans le gamme comprise entre 0.0005:1 et 0.05:1.

8. Procédé selon la revendication 1, caractérisé en ce que la réaction est menée à une température se situant dans la gamme comprise entre 20 et 200°C.

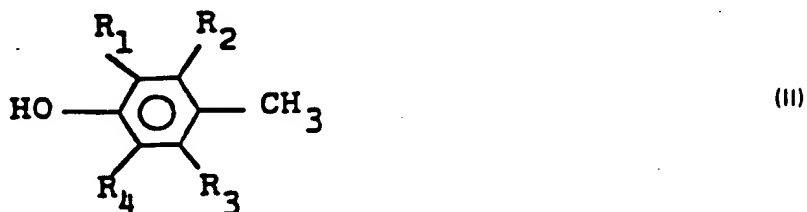
9. Procédé selon la revendication 1, caractérisé en ce que la réaction est menée avec l'air ou un mélange d'oxygène et d'azote en tant que gaz contenant de l'oxygène libre.

Patentansprüche

1. Verfahren zur Herstellung von 4-Hydroxybenzaldehyd-Derivaten der Formel



in der die Reste R_1 , R_2 , R_3 und R_4 jeweils ausgewählt sind aus der Gruppe Wasserstoffatom, Halogenatome, niedere Alkylreste, die Cyclohexylgruppe, niedere Alkoxyreste und die Cyclohexyloxygruppe, dadurch gekennzeichnet, daß man ein p-Cresol-Derivat der Formel



in der die Reste R_1 , R_2 , R_3 und R_4 die vorstehend angegebene Bedeutung haben, mit Sauerstoff oder einem freien Sauerstoff enthaltenden Gas in einem gegenüber Sauerstoff stabilen Lösungsmittel, das in der Lage ist, die Ausgangsverbindung zu lösen, in Gegenwart einer Base mit höherer Basizität als das p-Cresol-Derivat der Formel (II) und in Gegenwart einer katalytischen Menge einer Kobaltverbindung oder metallischem Kobalt, zur Umsetzung bringt.

2. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß man die Umsetzung mit p-Cresol, 2-Brom-p-cresol, 2-Chlor-p-cresol, 2,6-Dibrom-p-cresol, 2,6-Dichlor-p-cresol, 2,4-Xylenol, 3,4-Xylenol, Mesityl, 2-tert.-Butyl-p-cresol, 2,6-Di-tert.-butyl-p-cresol, 2-Methoxy-p-cresol, 2-Äthoxy-p-cresol oder 2,6-Dimethoxy-p-cresol als p-Cresol-Derivat durchführt.

3. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß man die Umsetzung mit Natriumhydroxid, Kaliumhydroxid, Natriummethoxid, Kaliummethoxid, Natriumäthoxid, Kaliumäthoxid, Kaliumtert.-butoxid oder Natriumamid als Base durchführt.

4. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß man die Umsetzung mit Kobalthydroxid, einem Kobaltoxid, Kobaltchlorid, Kobaltacetat, Kobaltsulfat oder Kobaltnitrat als Kobaltverbindung durchführt.

5. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß man die Umsetzung in Methanol, Athanol, Isopropanol, tert.-Butanol oder Äthylenglykol als Lösungsmittel durchführt.

6. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß man die Umsetzung mit einem Molverhältnis der Base zum p-Cresol-Derivat im Bereich von 1:1 bis 10:1 durchführt.

7. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß man die Umsetzung mit einer Kobaltverbindung oder metallischem Kobalt als Katalysator durchführt, und das Molverhältnis der Kobaltverbindung zum p-Cresol-Derivat oder das Verhältnis von metallischem Kobalt in Gram-Atomen zu Molen p-Cresol-Derivat im Bereich von 0,0005:1 bis 0,05:1 liegt.

8. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß man die Umsetzung bei einer Temperatur im Bereich von 20 bis 200°C durchführt.

9. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß man die Umsetzung mit Luft oder einem Gemisch aus Sauerstoff und Stickstoff als freien Sauerstoff enthaltenden Gas durchführt.